SYSTEM AND METHOD FOR CREATING TISSUE

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is a divisional of U.S. patent application Ser. No. 15/805,790 filed Nov. 7, 2017, now U.S. Publication No. US-2018-0127705-A1, published May 10, 2018 entitled System and Method for Applying Creating Tissue (Attorney Docket No. L81), which claims the benefit of U.S. Provisional Patent Application Ser. No. 62/418,784 filed Nov. 7, 2016, entitled System and Method for Applying Creating Tissue (Attorney Docket #S70), and U.S. Provisional Patent Application Ser. No. 62/534,984 filed Jul. 20, 2017, entitled Tissue Enclosure (Attorney Docket #V35), which are incorporated herein by reference in their entirety.

BACKGROUND

[0002] The present teachings relate generally to tissue engineering, and more specifically to systems and methods to enable tissue creation.

[0003] The current approach to growing structures in a granular gel bioreactor is to supply a fluid or pneumatic pressure gradient on an upstream reservoir or plenum to encourage flow through the granular gel and any cells or structures suspended in the gel. The flowing material could include nutrients and could wash away waste products from the structures. It might be optimal if the structures could remain positionally static while the nutrients flow through them. However, depending on the granular gel concentration, pressure amplitudes used, and other factors, the structures may only remain positionally static at a pressure gradient too low to provide a feasible flow rate of material. If the movement of the structures is too high, the structures may compress to a point where the cellular viability or future functionality of the tissue is compromised.

[0004] In 2016, approximately 119,000 people were on a waiting list for an organ transplant, and yet only 33,606 transplants occurred, an 8.5% increase over 2015. This disparity continues to grow. Tissue engineering and regenerative medicine seek to address this shortage by creating viable cells, tissues, and organs for transplantation in a controlled setting such as a bioreactor. These cells, tissues, and organs could potentially replace animal and human subjects for drug development and testing. In order to accomplish this goal, tissue engineering has turned to 3D tissue printing. Tissue printing uses living cells and other biological materials as bio-ink to produce a 3D structure. There are three categories of printing technologies used in this field: inkjet-based bioprinting, pressure-assisted bioprinting, and laser-assisted bioprinting.

[0005] In order to maintain the viability of the printed tissue structure, a steady supply of nutrients must enter a bioreactor that can house the printed tissue while waste exits from it. The field of tissue engineering faces the challenge of monitoring tissue production, which is crucial to ensuring that cells are growing and differentiating properly while receiving the appropriate nutrients and signals. However, monitoring developing tissue presents a unique challenge: obtaining high resolution images of developing cells and tissue in a non-invasive manner.

[0006] Creating human tissue can involve problems such as achieving the necessary precision in a timely way to create the tissue, and maintaining the viability of the tissue while it awaits use. Currently tissue engineering is primarily a manual and empirical process without a great deal of reproducibility or quality assurance. What is needed is a combination of state-of-the-art engineering solutions applied to the biological problems of creating and maintaining tissue.

[0007] One such technology is three-dimensional printing that can be used to print living cells, scaffolds for living cells, and/or complete organs. However, three-dimensionally printing even simple living tissues can require substantial improvements over current three-dimensional printing technology. Further, what is needed is a repeatable process so that the results of tissue creation can be predictable. Therefore, what is needed is a complete, automated system for creating tissue and maintaining its viability.

SUMMARY

[0008] The method of the present teachings for growing tissue can include, but is not limited to including, producing a protein associated with the tissue, selecting cells associated with the tissue, expanding the cells, creating at least one tissue bio-ink including the expanded cells, printing the at least one tissue bio-ink in at least one tissue growth medium mixture, growing the tissue from the printed at least one tissue bio-ink, and maintaining viability of the tissue. The method can optionally include maintaining the tissue, and packaging the tissue for transport. Producing the protein can include forming a recombinant protein precursor based on viral vectors associated with the tissue and cell lines associated with the tissue, forming disassociated protein precursor cells based on subjecting the recombinant protein precursor to at least one disassociation reagent and stress, creating at least one protein bio-ink based on the disassociated protein precursor cells and a sterile gel, creating at least one printable protein bio-ink based on the at least one protein bio-ink and at least one protein support material, printing the at least one printable protein bio-ink in at least one protein growth medium mixture, and growing the at least one printable protein bio-ink into the protein. The stress can include mechanical stress and fluid stress. The at least one protein growth medium can include the sterile gel, a sterile basal medium, and a recombinant protein. Expanding the cells can include forming disassociated tissue precursor cells based on subjecting the selected cells to at least one disassociation reagent and stress, creating a growth medium associated with growing the disassociated tissue precursor cells, forming a tissue precursor recombinant protein mixture based on the protein associated with the tissue and indicators and support materials associated with the disassociated tissue precursor cells, forming a cell/medium mixture of the disassociated tissue precursor cells, the growth medium, and the tissue precursor recombinant protein mixture, and growing the expanded cells in a bioreactor loaded with the cell/medium mixture. At least one tissue bio-ink can include the protein, tissue growth indicators, tissue growth factors, tissue support materials, and tissue gel. At least one tissue growth medium mixture can include the protein, tissue gel, and basal medium.

[0009] The system of the present teachings for growing tissue can include a protein production process producing a protein associated with the tissue, a cell selection process selecting cells associated with the tissue, a cell expansion process expanding the cells, and a build process creating